

## Some Aspects of the Problem of Adulterated Herbal Medicines by the Illegal Addition of Active Pharmaceutical Ingredients

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### Editorial

Counterfeit drugs have become a widespread threat to the public's health [1]. According to the World Health Organization (WHO) definition, a counterfeit drug is "a medicine which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging" [2]. Also U.S. Food and Drug Administration (FDA) defines a counterfeit drug as "a drug which, or the containers or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint or device or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed or distributed such drug and which thereby falsely purports or is represented to be product of or to have been packed or distributed by such other drug manufacturer, processor, packer, or distributor" [3]. Some counterfeit drugs contain active pharmaceutical ingredients with unknown doses [4]. WHO reported that about 10% of the global drug market is counterfeit. This is estimated up to 25-50% in developing countries [2,3].

Illegitimate manufacturers in herbal shops produce hand-made counterfeit herbal supplements without any quality and purity standards under the authority of regulatory systems. There is a great common concern that herbal drugs are safe without any side effects [5,6]. As a result of this belief many patients trust herbal supplement manufactures and rely on what they say about their products.

We should not neglect the safety aspects of adulterated opioid replacement therapy, anti-obesity, weight gain and sexual performance enhancement herbal supplements.

Unfortunately many countries struggle against drug abuse and its consequences. Therefore the demand for drugs used as opioid substitution therapy is high. Many drug dependent persons tend to use herbal supplements instead of synthetic drugs. But herbal shops add undeclared active pharmaceutical ingredients in hand made pharmaceutical dosage forms such as capsules, syrups, tablets and sachets. Counterfeit opioid substitution drugs often contain diphenoxylate, tramadol, codeine, sertraline, fluoxetine and acetaminophen to improve their effectiveness. According to the quantitative analyses results of these drugs in forensic toxicology laboratories in some instances they contain high doses of drugs that are dangerous for users [7]. Tramadol is a synthetic opioid that had been scheduled by the Drug Enforcement Administration (DEA) within the U.S [8]. Combining tramadol, fluoxetine and sertraline in a single dosage form can cause serotonergic syndrome due to the

combined action of tramadol and serotonin reuptake inhibitors at the neuronal synapse [9].

There are many reports that sibutramine, clenbuterol, nicotinamide, youhimbine, glybenclamide and ribonabant were detected in herbal weight loss supplements [10-14]. Also in the study of Kim et al. bisacodyl, sibutramine, ephedrine, pseudoephedrine and fluoxetine were the most frequent adulterants in weight loss food and dietary supplements [15]. Vaysse et al. reported that sibutramine was detected in some herbal medicines at doses ranging from 4.4-30.5 mg/capsule. Phenolphthalein and synephrine were other adulterants in herbal weight loss medicines [16].

Due to an increased risk of cardiovascular complications such as heart attack, non-fatal stroke and other heart related events, U.S. Food and Drug Administration (FDA) asked Abbot laboratories to withdraw sibutramine from U.S. drug market on October 8, 2010 [17].

Phenolphthalein is used in antiobesity drugs as a laxative. It should be taken into account that phenolphthalein produces free radicals leading to carcinogenesis [18].

The other problem is the use of adulterated weight gain drugs by athletics for muscle building and achieving a desired physical constitution. Wide ranges of active pharmaceutical ingredients are used in herbal supplements for weight gain. Anabolic steroids, glucocorticoids and cyproheptadine are used as adulterants in herbal medicines [19]. Glucocorticoids cause weight gain due to visceral and truncal fat deposition increase and appetite stimulation. The other side effects of glucocorticoids are hyperglycaemia that can be dangerous for diabetic users, increase skin fragility, and increase in intraocular pressure that should be considered in patients suffering from glaucoma and many other side effects [20,21].

There are some reports that sexual performance enhancement herbal medicines are adulterated with phosphodiesterase type-5 enzyme (PDE-5) inhibitors such as sildenafil [22-25]. Redness in the face and neck, indigestion, photophobia, blurred vision and in rare conditions ventricular arrhythmias, myocardial infarction and sudden hearing loss are side effects of constant sildenafil use [26].

In conclusion, counterfeit and adulterated herbal drugs that are mislabelled as "natural products" transfer a false sense of certainty to the patients with a potential for hidden risk of poisoning. The worldwide production of herbal supplements and drugs continues to increase, and there is growing demand for safe and effective drugs used to treat many diseases. Therefore it is necessary to set protocols from governmental healthcare authorities to control the production of counterfeit herbal medicines that may cause serious health problems for users.

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